REMARKS

Reconsideration is respectfully requested.

Status of the Claims

Claims 1-47 are pending. Because claims 3-10, 15-19, and 24-27 have been withdrawn from consideration, only claims 1, 2, 11-14, and 20-23 are at issue.

Finality of the Office Action

Applicants respectfully submit that the present Office Action has improperly been made final because the restriction requirement was not made or maintained in the previous Office Action.

In the Office Action dated September 27, 2006, the nonelected claims drawn to complex compositions containing the elected compounds and methods of making and using the elected compounds were rejoined to the application because the compounds were found to be allowable over the prior art. Accordingly, all claims in the application were pending and at issue.

"Rejoinder involves withdrawal of a restriction requirement between an allowable elected invention and a nonelected invention." MPEP § 821.04. Once the restriction requirement is withdrawn, the claims are no longer under restriction and the provisions of 35 U.S.C. § 121, including the protection against a double patenting rejection in a divisional application, do not apply. MPEP § 821.04(a). Therefore, the "re-restricting" of the claims in the present Office Action is in actuality a new restriction requirement only having the same form as the previous, withdrawn requirement.

Restriction "may be made at any time before final action." 37 C.F.R. § 1.142(a) (emphasis added); MPEP § 811. Because the present restriction requirement was not made or maintained in the previous Office Action, the present Office Action contains a new restriction requirement and should not have been made final.

Claim Rejections – 35 U.S.C. § 112

Claims 1, 2, 11-14, and 20-23 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly lacks enablement for analogs, tautomers, solvates, prodrugs, and stereoisomers of compounds 2-20.

Apparently referring to analogs and prodrugs of the principal compounds, the Examiner states, "It is not clear what these are as there are no examples or any guidance as to which compounds are included." However, Applicants respectfully submit that this is not true.

Concerning analogs, the specification states:

> In another embodiment, the compound according to formula 1 can be of different structural analogues such that structures 2 to 20 and their derivatives ma[y] have substitutions at C-1 or C-4, or C-5 or C-8 with substituted halogens (Br, I, F) or amine, amino, imino, carboxylic acid or amides."

(Specification at page 5, lines 2-6.) The Examiner also states that "[t]he analogs may not have the same activity." However, this is nothing more than pure speculation. Nothing in the record suggests that the analogs defined in the specification would not have the same activity as the core compounds claimed.

The specification also provides a number of examples and significant guidance regarding prodrugs of the principal compounds:

> "Prodrugs" are also encompassed by the present specification and are intended to include any covalently bonded carriers which release the active parent drug according to formula 1 to 20 in viva when such prodrug is administered to a mammalian subject. ... Prodrugs of a compound of formula 1 to 20 in Figure 2 above are prepared by

> modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or in vivo, to the parent compound. Prodrugs include compounds of formula 1 to 20 wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug or compound of formula 1 to 20 in Figure 2 above is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of formula 1 to 20 and the like.

(Specification at page 8, lines 8-20.)

The Examiner also states that "[c]laims employing functional language at the point of novelty, such as applicants', neither provide those elements required to practice the inventions, nor 'inform the public' during the life of the patent of the limits of the monopoly asserted." However, none of the "functional language" (presumably referring to the term "prodrug") is being used as a point of novelty in the claims as the Examiner asserts. Rather, the term describes the metes and bounds of the claimed derivatives of compounds that the Examiner has conceded are novel over the prior art.

Stereoisomers, tautomers, and pharmaceutically acceptable solvates are well-known and understood classes of derivatives that are frequently claimed in pharmaceutical inventions. *See, e.g.*, U.S. Patent No. 6,617,335 (claiming an alkaloid and its stereoisomers, tautomers, and solvates without further disclosure of how to make them). Furthermore, the specification, in fact, provides specific guidance as to how to make the claimed stereoisomers and examples of pharmaceutically acceptable solvates. "Additionally, modification of the stereochemistry of the above formulas is also within the skill of those in the art. For example, at C1 to C10 and from N1' to N9' and stereochemistry at C-4' can be either R- or S-." (Specification at page 6, lines 6-8.). "The structures of 1-20 illustrated in Figure 2 above are capable of forming pharmaceutically acceptable …

solvates, such as hydrates and alcoholates." (Specification at page 6, lines 13-15.) Tautomers are "structural isomers that exist in equilibrium and are readily converted from one isomeric form to another." ("Tautomer," Columbia Electronic Encyclopedia, 2007, *available at* http://columbia.thefreedictionary.com/Tautomer.). Where the principal compound is one isomer, its corresponding tautomeric isomer will naturally be present. The skilled artisan would readily appreciate this fact.

The Examiner further states that the availability of starting materials is a key issue in determining whether there is enablement and asserts that "there are no starting material[s] described." Apparently the Examiner asserts that the specification is not enabling because the product claims do not specify the starting materials for the process of making them. (If this is the case, Applicants point out that enablement is measured by the disclosure of the entire specification, not merely what is contained in the claims.)

The specification clearly teaches that the principal compounds (1-20) can be obtained by extraction from an ascidian, such as *Synoicum macrogalssum*. (*See, e.g.*, Specification at page 5, lines 19-21; page 11, lines 14-23.) Moreover, the specification discloses by example how to extract compounds of the present invention from the ascidian *Synoicum macrogalssum*. (Specification, beginning at page 11, line 27.) The claimed analogs, tautomers, solvates, prodrugs, and stereoisomers of the principal compounds are derived from those compounds. Applicants respectfully submit that the disclosure provides starting materials for the entire scope of the claims.

In applying the factors of *In re Wands*, the Examiner determines that the claims "encompass many compounds with the [metes] and bounds unclear" and that the invention is "a (highly) substituted compound." However, enablement is a test of whether the disclosure teaches the skilled artisan to make and use the invention commensurate in scope with the claims. To make a determination of enablement the scope of the claims must be clear. Applicants submit that if the scope of the claims is unclear to the Examiner, an enablement rejection cannot be properly made. Applicants invite the Examiner to seek clarification where clarity may be lacking.

Applicants also respectfully submit that the claims encompass far fewer compounds than typically claimed in an issued chemical patent and the compound is far from being highly substituted. The compounds are not defined by many Markush groups having numerous possible substituents. The formula of claim 2 comprises (a) a single core structure with an alkyl chain having 2 to 6 carbon atoms and (b) two positions Q and R_1 each having two possible substituents—which amounts to a total of twenty compounds. The bounds of the claimed derivatives are defined by well-known and commonly used terms for derivatives of chemical compounds (*see* "stereoisomers," "tautomers," and "pharmaceutically acceptable solvates") and by terms defined in the specification (*see* "analog" and "prodrug").

The Examiner also determines that unpredictability is very high because "[t]here is very little known about prodrugs, solvates, analogs, tautomers, [and] stereoisomers. With so many variables and definitions [whose] [metes] and bounds [are] unclear and described by functional language." Again, Applicants offer to clarify what the Examiner finds to be unclear and respectfully submit that the claimed derivatives are defined in the specification or sufficiently well-known in the art such that the skilled artisan could readily envision the scope of the claims.

The Examiner notes that "[t]he inventor provides no direction in the instant specification. There are no examples drawn to prodrugs, solvates, tautomers, analogs, [and] stereoisomer[] groups" and that "[t]he instant specification does not have any working examples." Applicants submit, as noted above, that the inventors have provided ample direction concerning how to make and use analogs, prodrugs, and stereoisomers. Applicants also note that the specification does not contain any working examples directed to pharmaceutically acceptable salts of the principal compounds. However, as the Examiner agrees, the teaching of the specification combined with the general knowledge in the art enables the skilled artisan to make and use salts of the principal compounds. Applicants submit that due to the knowledge in the art regarding the other claimed derivatives and the direction provided by the specification, the other derivatives are similarly enabled.

Finally, the Examiner refers to the following from *Genentech, Inc. v. Novo Nordisk*, 108 F.3d, 42 USPQ2d 1001 (Fed. Cir. 1997):

> Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

In *Genentech*, the court stated that "[the patentee] is attempting to bootstrap a vague statement of a problem into an enabling disclosure sufficient to dominate someone else's solution of the problem." Here, Applicants do not rely on "vague intimations" and "general ideas." Applicants have particularly defined certain principal compounds and derivatives that are either produced in the same extraction procedure or can be obtained by minor modifications that are within the capability of the skilled artisan.

For at least the above reasons, Applicants submit that, based on the present disclosure, the skilled artisan could modify the principal compounds to make and use the entire scope of the claimed derivatives without departing from the spirit of the invention. Withdrawal of the rejection and allowance of the claims are respectfully requested.

CONCLUSION

In view of the above remarks, Applicants believe the pending application is in condition for allowance. If there are any remaining issues that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is kindly requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

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